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Abstract

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PI Title:

Project Title: DIET, ENDOTHELIAL FUNCTION AND PEDIATRIC
HYPERLIPIDEMIA

Abstract: Coronary heart disease (CHD) remains the leading cause of death in the United States. The pathogenesis of atherosclerosis and CHD is thought to be initiated by endothelial dysfunction or injury. Factors that contribute to oxidative stress such as elevated cholesterol-rich low density and very low-density lipoproteins (LDL and VLDL) result in endothelial dysfunction. The long term goal of this proposal is to develop dietary interventions for the prevention and treatment of endothelial dysfunction in children and adolescents who are at high risk for premature CHD due to the genetic lipid disorders of familial hypercholesterolemia (FH) or familial combined hyperlipidemia (FCH). This experimental, randomized, double blind crossover, placebo-controlled clinical trial will include 96 hyperlipidemic children and adolescents aged 10 to 18 years who will receive dietary supplements and an intensive dietary educational program. The following hypothesis will be evaluated: Specific nutrients in the diet will have direct beneficial vascular effects and/or indirect effects on lipoprotein composition which will in turn decrease the oxidation of LDL and the level of vascular oxidative stress, thereby improving endothelial function. The primary specific aims are: 1) to determine whether a National Cholesterol Education Program (NCEP) Step II diet alone or together with one of four putative vasculoprotective supplements (Vitamins C & E, w-3 fatty acids, L-arginine, folic acid) will improve endothelial function in children and adolescents with FH and FCH, and 2) to evaluate the effects of these supplements on plasma lipoprotein profiles, LDL composition, lipoprotein-associated antioxidant enzymes (paraoxonase and platelet activating factor acetyl hydrolase), indices of oxidative stress (oxidized LDL, 8-hydroxy-2'-deoxyguanosine), immune function (inflammatory cytokines, plasma adhesion molecules),

and blood pressure. Vascular reactivity, a sensitive indicator of endothelial function, will be measured noninvasively using high-resolution external vascular ultrasound of the brachial artery. The secondary aims are: 1) to examine children and adolescents psychological well being, beliefs and feelings about their cardiovascular status and its relation to health outcomes, and 2) To explore their practices and health risk behaviors specifically in the area of dietary adherence. These studies will provide important insight into the mechanism of endothelial dysfunction and should serve to identify potential treatments for pediatric hyperlipidemia. Preventive nursing strategies aimed at early detection of endothelial dysfunction and dietary modification may restore endothelial function in children and adolescents at high risk for CHD.

Thesaurus Terms:

adolescence (12-18), cardiovascular disorder prevention, diet therapy, dietary supplement, human therapy evaluation, hypercholesterolemia, hyperlipidemia, middle childhood (6-11), vascular endothelium
arginine, ascorbate, blood pressure, cardiovascular disorder education, child behavior, clinical trial, folate, low density lipoprotein, omega 3 fatty acid, outcomes research, quality of life, therapy compliance, tocopherol
clinical research, human subject, nutrition related tag

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